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Prevalence of malignant hyperthermia diagnosis in hospital discharge records in California, Florida, New York, and Wisconsin

Zhen Lu [a], Henry Rosenberg [b], Guohua Li [a,c,*]

[a] Department of Epidemiology, Columbia University Mailman School of Public Health, 722 West 168th St, R1508, New York, NY 10032, USA
[b] Department of Medical Education and Clinical Research, Saint Barnabas Medical Center, 94 Old Short Hills Road, Livingston, NJ 07039, USA
[c] Department of Anesthesiology, Columbia University College of Physicians and Surgeons, 622 West 168th St, PH5-505, New York, NY 10032, USA

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ABSTRACT

Study objective: Malignant hyperthermia (MH) is a rare yet potentially fatal pharmacogenetic disorder triggered by exposure to inhalational anesthetics and the depolarizing neuromuscular blocking agent succinylcholine. Epidemiologic data on the geographic variation in MH prevalence is scant. The objective of this study is to examine the prevalence of recorded MH diagnosis in patients discharged from hospitals in four states in the United States.
Design: Observational study.
Setting: Healthcare Cost and Utilization Project (HCUP) State Inpatient Database (SID) for California (2011), Florida (2011), New York (2012) and Wisconsin (2012).
Patients: A total of 164 hospital discharges that had a recorded diagnosis of MH using the International Classification of Disease, 9th Revision, Clinical Modification code 995.86.
Methods: MH prevalence was assessed by patient demographic and clinical characteristics.
Main results: The prevalence of MH per 100,000 hospital discharges ranged from 1.23 (95% Confidence Interval [CI], 0.80–1.66) in New York to 1.91 (95% CI, 1.48–2.34) in California, and the prevalence of MH per 100,000 surgical discharges ranged from 1.47 (95% CI, 0.93–2.02) in New York to 2.86 (95% CI, 2.00–3.71) in Florida. The prevalence of MH in male patients was more than twice the prevalence in female patients. Of the 164 patients with MH diagnosis, 11% were dead on discharge.
Conclusions: There exists a modest variation in the prevalence of recorded MH diagnosis in hospital discharges in California, Florida, New York and Wisconsin. Epidemiologic patterns of MH diagnosis in hospital discharges appear to be similar across the four states. Further research is needed to better understand the geographic variation and contributing factors of MH in different populations.

1. Introduction

Malignant Hyperthermia (MH) is an autosomal-dominant genetic disorder of the skeletal muscle, in many cases linked to mutations in RYR1 and CACNA1S genes [1,2]. This pharmacogenetic clinical syndrome is triggered by sensitivity to volatile inhalational anesthetic gases (e.g., sevoflurane, desflurane, isoflurane, etc.) and the depolarizing neuromuscular blocking agent succinylcholine, leading to skeletal muscle hypermetabolism [3]. Epidemiologic data on MH are scant in the U.S. The prevalence of MH due to anesthetics is estimated to range from 1 per 16,000 in Denmark [4] to 1 per 100,000 in New York State [5]. MH is reported to affect all racial groups though regional variation of prevalence in MH susceptibility and prevalence have been noted worldwide [1,4–7]. The true prevalence of MH is hard to define due to unrecognized mild or aborted reactions, and the variable penetrance of the inherited susceptibility [8].

The prevalence of MH in hospital discharges across the United States has been estimated to be approximately 1 per 100,000 [5,8,9]. Factors associated with elevated MH risk include male sex, young age, several myopathies and congenital anomalies [5,9,10]. MH susceptibility as diagnosed with a caffeine-halothane contracture has been documented in patients with heat stroke and exercise-induced rhabdomylosis [11–14].

There is little information on the epidemiological pattern of MH across geographic regions in the United States. There is anecdotal evidence for excess MH risk in Florida [15] and Wisconsin [14]. In particular, it has been reported that residents of north-central Wisconsin may have higher MH susceptibility [16]. However, there have been no epidemiologic studies examining the prevalence of MH in these specific states. The purpose of this study is to better understand the

* Corresponding author at: Department of Anesthesiology, Columbia University College of Physicians and Surgeons, 622 West 168th St, PH5-505, New York, NY 10032, United States.
E-mail addresses: katherinezhenlu@gmail.com (Z. Lu), HRosenberg@barnabashealth.org (H. Rosenberg), GL2240@cumc.columbia.edu (G. Li).

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epidemiology of MH in the United States by estimating the prevalence of MH diagnosis and characterize factors associated with MH diagnosis recorded in a large sample of inpatient database in four states located in different US geographic regions, including California in the West, Florida in the South, New York in the Northeast, and Wisconsin in the Midwest.

2. Materials and methods

This study meets the criteria for the Protection of Human Subjects exemption 4 (research involving pre-existing data) of the U.S. Code of Federal Regulations (45 CFR 46.101). The study was deemed exempt from review by the institutional review board's Administrative Review Committee at the Columbia University Medical Center (New York, New York).

2.1. Data source

Data for this study came from the Healthcare Cost and Utilization Project (HCUP) State Inpatient Database (SID) for California (2011), Florida (2011), New York (2012) and Wisconsin (2012) (most recently available data at the time of the study), which are composed of annual, state-specific files that share uniform structure and data elements that facilitate cross-state comparisons [17]. The SID contains inpatient discharge records from within a state, including abstracts from community hospitals and non-community hospitals. Community hospitals, as defined by the American Hospital Association (AHA), include "all nonfederal, short-term, general and other specialty hospitals, excluding hospital units of institutions". Non-community hospitals include federal hospitals, long-term hospitals, psychiatric hospitals, alcohol/chemical dependency treatment facilities and hospital units within institutions such as prisons [18]. The database contains clinical and nonclinical information on all patients including patient diagnoses and procedures, admission and discharge status, patient demographics (e.g., gender, age, and race), payment source (Medicare, Medicaid, private insurance, and uninsured) and some hospital characteristics. The SID are discharge-level (not patient) files in which each record represents one inpatient visit. The Agency for Healthcare Research and Quality aggregates ICD-9-CM diagnostic coding into meaningful clinical groups: the Clinical Classification Software (CCS) codes [19].

2.2. Study sample

The study sample consisted of all inpatient discharges in California during 2011, Florida during 2011, New York during 2012, and Wisconsin during 2012. MH cases were identified by screening all the discharge diagnoses using the ICD-9-CM code 995.86 to indicate MH events as well as MH susceptibility. We calculated the prevalence of MH based on two denominators: (1) all hospital discharges; (2) hospital discharge with a surgical ICD-9 procedure code listed [20]. The two risk groups were not mutually exclusive.

2.3. Statistical analysis

Prevalence of MH due to anesthesia was calculated based on all inpatient discharges in the SID for four states. MH prevalence in hospital and surgical discharges among four states was examined according to patient demographic characteristics including age, sex, admission type and comorbid conditions. Comorbidities were identified by applying the Charlson Comorbidity Score to ICD-9-CM codes in the datasets [21,22]. Descriptive statistics such as 95% confidence interval (CI) and standard errors were calculated using inpatient discharges from each state as the denominator and MH discharges of each state as the numerator. Comparisons of prevalence among different patient groups were performed with SAS version 9.4 (SAS Institute, Cary, NC) using χ^2 test to compare categorical variables. Statistical significance was defined as $P < 0.05$ with Bonferroni correction for multiple comparisons.

3. Results

3.1. Prevalence

The SID for all four states contained a total of 9,745,539 inpatient discharge records, including 164 having an MH diagnosis. The overall prevalence of MH was 1.68 (95% CI, 1.42–1.94) per 100,000 hospital discharges and 2.37 (95% CI, 1.99–2.75) per 100,000 surgical discharges. Higher MH prevalence was observed in surgical discharges compared to hospital discharges across all four states (Fig. 1). The prevalence of MH diagnosis did not differ significantly across the states for all hospital discharges ($P > 0.90$) and for surgical discharges ($P = 0.16$) (Fig. 1). California had the highest prevalence of MH diagnosis for all hospital discharges (1.91 per 100,000; 95% CI, 1.48–2.34) while Florida had the highest prevalence of MH diagnosis for surgical discharges (2.86 per 100,000; 95% CI, 2.00–3.71) (Fig. 1).

The prevalence of MH was significantly higher in males and young adults than in females and older adults, respectively (Table 1). The prevalence of MH per 100,000 hospital discharges was similar across racial groups (Table 1). The prevalence of MH for surgical discharges was 5.8 times (95% CI, 3.33–9.95) that for non-surgical discharges (Table 1).

The variable indicating any exposure to anesthesia was only available for New York. In New York State alone, the prevalence of MH was 4.52 (95% CI, 2.06–6.98) per 100,000 discharges exposed to general anesthesia, 0.27 (95% CI, 0.00–0.79) per 100,000 discharges exposed to other anesthesia including local and regional anesthesia, and 0.88 (95% CI, 0.36–1.40) per 100,000 discharges exposed to no anesthesia (data not shown).

3.2. Characteristics of MH cases

Of the 164 patients with a diagnosis of MH, 47.6% were aged 44 years or younger with the median age of 46.5 years, 59.4% were white, 60.7% were male, and 91.5% were surgical discharges (Table 1). Among the four states studied, California did not collect data on the type of admission (emergency, urgent, elective, etc.). For the three other states, 65.9% of cases with an MH diagnosis were admitted as emergency or urgent types. Based on the Charlson-Deyo Comorbidity Score ≥ 1, 37.2% of the MH cases had at least one significant pre-existing medical condition (Table 1). Of all the hospital discharges, the prevalence of MH did not differ significantly by patient race, Charlson-Deyo Comorbidity Index and admission type (Table 1). It was shown that among patient discharges recorded with MH diagnosis, 11.0% were dead on discharge (Table 1).

Multivariable logistic regression analyses identified age, sex, and state as significant and independent factors associated with prevalence of MH diagnosis for the first denominator, all hospital discharges

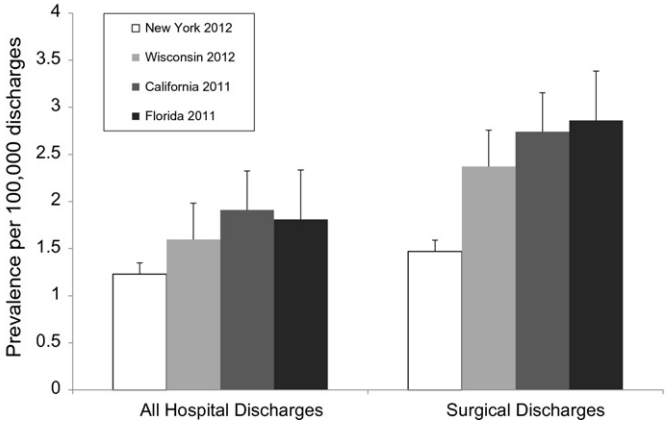

Fig. 1. Prevalence and standard error of malignant hyperthermia (MH) per 100,000 discharges by state and denominator type.